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     (FILE 'HOME' ENTERED AT 15:29:30 ON 25 JUN 2003)

     FILE 'EUROPATFULL, PATDPAFULL, PCTFULL, RDISCLOSURE, USPATFULL, USPAT2,
     WPIDS' ENTERED AT 15:30:05 ON 25 JUN 2003
                E WOLFFGRAMM J/IN
L1            5 S E3-E5

     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 16:23:42 ON 25 JUN 2003
                E WOLFFGRAMM/AU
L2          100 S E4-E5
L3            1 S L2 AND CORTICOSTEROID#
L4           35 S L2 AND ADDICT?
L5           16 S L4 NOT PY>=1998

     FILE 'STNGUIDE' ENTERED AT 16:35:15 ON 25 JUN 2003

     FILE 'EUROPATFULL, PATDPAFULL, PCTFULL, RDISCLOSURE, USPATFULL, USPAT2,
     WPIDS' ENTERED AT 16:37:09 ON 25 JUN 2003
L6         24228 S CORTICOSTERONE OR PREDNISOLONE OR PREDNISONE OR
PREDNYLIDENE
L7        235856 S OPIOID OR OPIATE OR NICOTINE OR CANABINOID OR AMPHETAMINE
OR
L8         30436 S OPIOID OR OPIATE OR NICOTINE OR CANABINOID OR AMPHETAMINE
OR
L9          3384 S L6(L)L7
L10          433 S L9(L)ADDICT?
L11           61 S L10 NOT PY>=1998
L12           61 DUP REM L11 (0 DUPLICATES REMOVED)

     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 17:17:29 ON 25 JUN 2003
L13           61 S L11
L14           23 DUP REM L13 (38 DUPLICATES REMOVED)

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disclosed in US patent nos. 2,789,118, 2,990,401, 3,048,581, 3,126,375, 3@929@768@ 3@996,359, 3,928,326 and 3,749,712. **Dexamethasone** (Decadron TM) is particularly preferred. Furthermore, a compound of formula (1) may be administered in combination with a chemotherapeutic agent such

5 ANSWER 1 OF 7 PCTFULL COPYRIGHT 2003 Univentio

ACCESSION NUMBER: 1998042275 PCTFULL ED 20020514

TITLE (ENGLISH): METHOD OF TREATMENT OF MIGRAINE

TITLE (FRENCH): TRAITEMENT DE LA MIGRAINE

INVENTOR(S): PEYMAN, Gholam, A.

PATENT ASSIGNEE(S): ADOLOR CORPORATION

LANGUAGE OF PUBL.: English

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9842275	A1	19981001

DESIGNATED STATES

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.: WO 1998-US5680 A 19980324

PRIORITY INFO.: US 1997-8/828,144 19970324

L6 ANSWER 1 OF 5 PCTFULL COPYRIGHT 2003 Univentio
ACCESSION NUMBER: 1995022963 PCTFULL ED 20020514
TITLE (ENGLISH): DRUG TARGETING SYSTEM, METHOD FOR PREPARING SAME AND ITS USE
TITLE (FRENCH): SYSTEME DE CIBLAGE D'UN MEDICAMENT, PROCEDE DE PREPARATION ET UTILISATION DE CE MEDICAMENT
INVENTOR(S): KREUTER, Joerg;
KARKEVICH, Dimitri A.;
SABEL, Bernhard;
ALYAUTDIN, Renad N.
PATENT ASSIGNEE(S): MEDINOVA MEDICAL CONSULTING GMBH
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9522963	A1	19950831

DESIGNATED STATES
W: AU CA HU JP AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1995-EP724 A 19950228
PRIORITY INFO.: US 1994-8/203,326 19940228

L6 ANSWER 2 OF 5 PCTFULL COPYRIGHT 2003 Univentio
ACCESSION NUMBER: 1994014462 PCTFULL ED 20020513
TITLE (ENGLISH): METHOD OF RETARDING THE PROGRESSION OF CHRONIC RENAL FAILURE
TITLE (FRENCH): PROCEDE DE RETARDEMENT DE LA PROGRESSION D'UNE INSUFFISANCE RENALE CHRONIQUE
INVENTOR(S): WALSER, Mackenzie
PATENT ASSIGNEE(S): WALSER, Mackenzie
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9414462	A1	19940707

DESIGNATED STATES
W: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1993-US12437 A 19931221
PRIORITY INFO.: US 1992-996,757 19921224

L6 ANSWER 3 OF 5 USPATFULL
ACCESSION NUMBER: 97:44769 USPATFULL
TITLE: Subcutaneous implant
INVENTOR(S): Grossman, Stuart A., Towson, MD, United States
Leong, Kam W., Ellicott City, MD, United States
Lesser, Glenn J., Baltimore, MD, United States
Lo, Hungnan, Baltimore, MD, United States
PATENT ASSIGNEE(S): Axxia Technologies, Bethesda, MD, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5633000		19970527	
APPLICATION INFO.:	US 1994-264689		19940623	(8)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Mullis, Jeffrey C.

LEGAL REPRESENTATIVE: Nixon & Vanderhye P.C.
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 13 Drawing Figure(s); 10 Drawing Page(s)
LINE COUNT: 782
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 4 OF 5 USPATFULL
ACCESSION NUMBER: 89:65118 USPATFULL
TITLE: Treatment of mammals suffering from damage to the central nervous system
INVENTOR(S): Naftchi, Nosrat E., 389 Forest Ave., Teaneck, NJ, United States 07666

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4855325		19890808
APPLICATION INFO.:	US 1988-150767		19880201 (7)

DISCLAIMER DATE: 20050503
RELATED APPLN. INFO.: Division of Ser. No. US 1985-691830, filed on 16 Jan 1985, now patented, Pat. No. US 4742054 which is a continuation of Ser. No. US 1982-443915, filed on 23 Nov 1982, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Rollins, John W.
LEGAL REPRESENTATIVE: Magidoff, Barry G.
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
LINE COUNT: 546
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 5 OF 5 USPATFULL
ACCESSION NUMBER: 88:27758 USPATFULL
TITLE: Treatment of mammals suffering from damage to the central nervous system
INVENTOR(S): Naftchi, Nosrat E., 389 Forest Ave., Teaneck, NJ, United States 07666

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4742054		19880503
APPLICATION INFO.:	US 1985-691830		19850116 (6)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1982-443915, filed on 23 Nov 1982, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Brown, J. R.
ASSISTANT EXAMINER: Rollins, Jr., John W.
LEGAL REPRESENTATIVE: Magidoff, Barry G.
NUMBER OF CLAIMS: 23
EXEMPLARY CLAIM: 1
LINE COUNT: 581
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 1 OF 7 PCTFULL COPYRIGHT 2003 Univentio

DETD . . . are difficult to treat. Also, stronger analgesics which act on the central nervous system, including morphine and pethicline .(meperidine) have risks of **addiction** and their systemic administration generally is contraindicated for treatment of migraine.

The methods of the invention further include a method of treatment of migraine comprising the topical administration of an **opioid**, in combination with the administration of an antiinflammatory compound. Antiinflammatory compounds include steroids, particularly glucocorticoids, for example, cortisol, cortisone, **prednisolone**, clexamethasone and the like; and nonsteroids, particularly salicylates (such as aspirin), pyrazolon derivatives (such as phenylbutazone), indomethacin and sulindac, fenamates, and propionic. . .

CLMEN. . . for treatment of CNS disorders include:
Drugs acting at synaptic and neuroeffector junctional sites; general and
local
analgesics and anesthetics such as **opioid** analgesics and
antagonists; hypnotics and sedatives;
drugs for the treatment of psychiatric disorders such as depression,
schizophrenia; anti-
epileptics and anticonvulsants; Huntington's. . . factor, or nerve
growth factor; drugs aimed at the treatment of CNS'
trauma or stroke; and drugs for the treatment of **addiction** and
drug abuse; autacoids and anti-
inflammatory drugs; chemotherapeutic agents for parasitic infections and
microbial diseases;
immunosuppressive agents and anti-cancer drugs; hormones. . .
adrenergic
agonists, adrenergic receptor antagonists, transmitters such as GABA,
glycine, glutamate,
acetylcholine, dopamine, 5-hydroxytryptamine, and histamine, neuroactive
peptides;
analgesics and anesthetics such as **opioid** analgesics and
antagonists;
preanesthetic and anesthetic medications such as benzodiazepines,
barbiturates,
antihistamines, phenothiazines and butylphenones; **opioids**;
antiemetics; anticholinergic
drugs such as atropine, scopolarnine or glycopyrrolate; cocaine; chloral
derivatives;
ethchlorvynol; glutethimide; methyprylon; meprobamate; paraldehyde;
disulfiram; morphine,
fentanyl and naloxone;
centrally active. . . or
SUBSTITUTE SHEET (RULE 26)
- 13 -
nerve growth factor; neurotrophine(NT) 3 (NT3); NT4 and NT5;
gangliosides;
neuroregenerative agents;
drugs for the treatment of **addiction** and drug abuse include
opioid antagonists
and anti-depressants;
autocoids and anti-inflarnmatory drugs such as histamine, bradykinin,
kallidin
and their respective agonists and antagonists;
chemotherapeutic agents for parasitic infections and. . . mineral or
nutritional agents, anti-obesity drugs, anabolics
and anti-asthmatics, anti-inflammatory drugs such as phenylbutazone,
indomethacin,
naproxen, ibuprofen, flurbiprofen, diclofenac, dexamethasone, prednisone
and **prednisolone**;
cerebral vasodilators such as soloctidilum, vincamine, naftidrofaryl
oxalate, co-dergocrine
mcsylate, cyclandelate, papaverine, nicotinic acid, anti-infective
agents such as erythromycin
stearate, and cephalexin.
Mechanism of. . . are

modulated b various factors, including some substances, like leucine and
aluminum Banks,
y
W.A., Kastin, A.J., Editorial review: Peptide transport system for **opiates** across the blood-
brainbarrier.Am.J.Physiol.,M:EI-EIO(1990). Whethertransportmechanismsof nanoparticles are similar to transport of peptides is not known currently. As the present
invention is the first. . .
. . .
neurotropic factors and
neuroregenerative agents; trophic factors; drugs aimed at the treatment of CNS
trauma or stroke; drugs for the treatment of **addiction** and
drug abuse; autacoids and
anti-inflammatory drugs; chemotherapeutic agents for parasitic infections and
microbial diseases; immunosuppressive agents and anti-cancer drugs; hormones and
hormone. . .
. . .
factors and neuroregenera-
tive agents; trophic factors; drugs aimed at the treatment of CNS trauma
or stroke;
drugs for the treatment of **addiction** and drug abuse; autacoids and anti-inflammatory
drugs; chemotherapeutic agents for parasitic infections and microbial diseases;
immunosuppressive agents and anti-cancer drugs; hormones and. . .

L5 ANSWER 2 OF 7 PCTFULL COPYRIGHT 2003 Univentio

ACCESSION NUMBER: 1998029101 PCTFULL ED 20020514

TITLE (ENGLISH): PHARMACEUTICAL PREPARATIONS OF GLUTATHIONE AND METHODS OF ADMINISTRATION THEREOF

TITLE (FRENCH): PREPARATIONS PHARMACEUTIQUES DE GLUTATHION ET MODES D'ADMINISTRATION DE CES PREPARATIONS

INVENTOR(S): DEMOPOULOS, Harry, B.;
SELIGMAN, Myron, L.

PATENT ASSIGNEE(S): ANTIOXIDANT PHARMACEUTICALS CORPORATION;
DEMOPOULOS, Harry, B.;
SELIGMAN, Myron, L.

LANGUAGE OF PUBL.: English

DOCUMENT TYPE: Patent

PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9829101	A1	19980709

DESIGNATED STATES
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN GH GM KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.: WO 1997-US23879 A 19971231

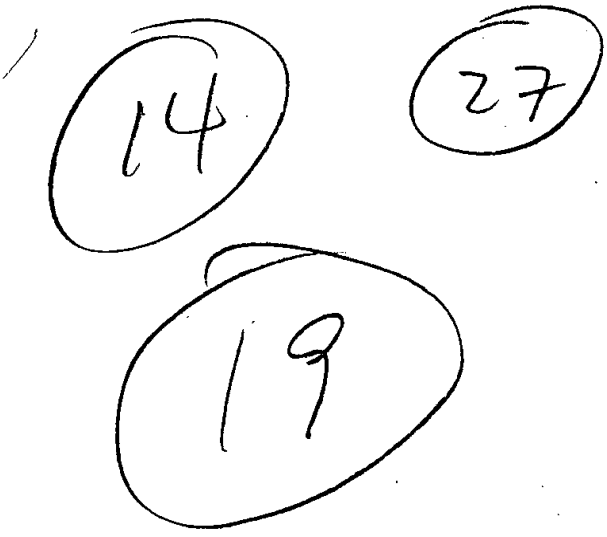
PRIORITY INFO.: US 1996-60/034,101 19961231

L12 ANSWER 14 OF 61 PCTFULL COPYRIGHT 2003 Univentio
ACCESSION NUMBER: 1997010827 PCTFULL ED 20020514
TITLE (ENGLISH): USE OF ANTIMINERALOCORTICOID COMPOUNDS AGAINST DRUG WITHDRAWAL SYNDROME
TITLE (FRENCH): UTILISATION DES COMPOSES ANTIMINERALOCORTICOIDES CONTRE
LE SYNDROME DE SEVRAGE DES NARCOTIQUES
INVENTOR(S): PETIT, Francis;
PHILIBERT, Daniel;
GOEDERS, Nick
PATENT ASSIGNEE(S): ROUSSEL UCLAF;
PETIT, Francis;
PHILIBERT, Daniel;
GOEDERS, Nick
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9710827	A1	19970327

DESIGNATED STATES
W: JP US AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
APPLICATION INFO.: WO 1996-FR1459 A 19960919
PRIORITY INFO.: FR 1995-95/11086 19950921

DETD . . . a mis en Evidence l'application nouvelle



L12 ANSWER 12 OF 61 PCTFULL COPYRIGHT 2003 Univentio
ACCESSION NUMBER: 1997018206 PCTFULL ED 20020514
TITLE (ENGLISH): MORPHOLINE DERIVATIVES AND THEIR USE AS THERAPEUTIC AGENTS
TITLE (FRENCH): DERIVES DE LA MORPHOLINE ET LEUR UTILISATION COMME AGENTS THERAPEUTIQUES
INVENTOR(S): SWAIN, Christopher, John;
TEALL, Martin, Richard;
WILLIAMS, Brian, John
PATENT ASSIGNEE(S): MERCK SHARP & DOHME LIMITED;
SWAIN, Christopher, John;
TEALL, Martin, Richard;
WILLIAMS, Brian, John
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

NUMBER	KIND	DATE
WO 9718206	A1	19970522

DESIGNATED STATES
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN KE LS MW SD SZ UG AM AZ BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN TD TG

APPLICATION INFO.:	WO 1996-GB2766	A	19961113
PRIORITY INFO.:	GB 1995-9523244.3		19951114

DETD . . . as angina and Reynauld's disease, fibrosing and collagen diseases such as scleroderma and eosinophilic fascioliasis, reflex sympathetic dystrophy such as shoulder/hand syndrome, **addiction** disorders such as alcoholism, stress related somatic disorders, neuropathy, neuralgia, disorders related to immune enhancement or suppression such as systemic lupus erythmatosus (European. . . .

malignant syndrome, neuroleptic-induced acute dystonia, neuroleptic-induced acute akathisia, neuroleptic-induced tardive dyskinesia and medication-induced postural tremour; substance-related disorders arising from the use of alcohol, **amphetamines** (or **amphetamine**-like substances) caffeine, cannabis, **cocaine**, hallucinogens, inhalants and aerosol propellants, **nicotine**, opioids, phenylglycidine derivatives, sedatives, hypnotics, and anxiolytics, which substance-related disorders include dependence and abuse, intoxication, withdrawal, intoxication delerium, withdrawal delerium, persisting dementia, psychotic. . . .

agonists such as baclofen. Additionally, a compound of formula (I) may be administered in combination with an anti-inflammatory corticosteroid, such as **dexamethasone**, triamcinolone, triameinolone acetonide, flunisolide, budesonide, or others such as those

L22 ANSWER 14 OF 34 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:448816 CAPLUS
DOCUMENT NUMBER: 109:48816
TITLE: Prolactin release induced by opiate agonists: Effect of glucocorticoid pretreatment in intact and adrenalectomized rats
AUTHOR(S): Kiem, Do Thanh; Kanyicska, Bela; Stark, Ervin; Fekete, Marton I. K.
CORPORATE SOURCE: Inst. Exp. Med., Hungarian Acad. Sci., Budapest, H-1450, Hung.
SOURCE: Neuroendocrinology (1988), 48(2), 174-9
CODEN: NUNDAJ; ISSN: 0028-3835
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Cortisol** (25 **mg**/kg) administered 24 h before measurements decreased the prolactin secretion induced by intraventricularly given **opioids** (dynorphin, beta-endorphin, Met-enkephalin, or D-Met-Pro-enkephalinamide). The effect of cortisol was depressed by actinomycin D pretreatment. The cortisol-induced inhibition of the action of morphine was facilitated in adrenalectomized animals; a maximal inhibition was obtained at a dose of 5 mg/kg. The opioid-induced corticosterone secretion was not affected 24 h after a single administration of cortisol. The cortisol-induced inhibition of opioid-induced prolactin secretion is dependent on protein synthesis and independent of changes in drug metab., and of the type of opiate receptor preferentially affected by the opiate agonists employed.

AB **Cortisol** (25 **mg**/kg) administered 24 h before measurements decreased the prolactin secretion induced by intraventricularly given **opioids** (dynorphin, beta-endorphin, Met-enkephalin, or D-Met-Pro-enkephalinamide). The effect of cortisol was depressed by actinomycin D pretreatment. The cortisol-induced inhibition of the action of morphine was facilitated in adrenalectomized animals; a maximal inhibition was obtained at a dose of 5 mg/kg. The opioid-induced corticosterone secretion was not affected 24 h after a single administration of cortisol. The cortisol-induced inhibition of opioid-induced prolactin secretion is dependent on protein synthesis and independent of changes in drug metab., and of the type of opiate receptor preferentially affected by the opiate agonists employed.

L22 ANSWER 19 OF 34 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1988:49530 CAPLUS
DOCUMENT NUMBER: 108:49530
TITLE: Corticosteroid effects on morphine-induced antinociception as a function of two types of corticosteroid receptors in brain
AUTHOR(S): Ratka, A.; Veldhuis, H. D.; De Kloet, E. R.
CORPORATE SOURCE: Med. Fac., Univ. Utrecht, Utrecht, 3521, Neth.
SOURCE: Neuropharmacology (1988), 27(1), 15-21
CODEN: NEPHBW; ISSN: 0028-3908
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Adrenalectomy sensitized rats to the analgesic effect of morphine and .beta.-endorphin. Replacement therapy (chronic and acute) with corticosterone, dexamethasone, or RU 28362 (glucocorticoid receptor agonist) effectively reversed the increase in the sensitivity to the analgesic effect of peripherally injected morphine (5 mg/kg i.p.) induced by adrenalectomy to the level of sham-operated animals. Glucocorticosteroids administered to nonadrenalectomized rats did not change the sensitivity to morphine. Corticosterone had a biphasic, dose-dependent effect; the most significant attenuation of the hypersensitivity to morphine-induced antinociception in adrenalectomized rats was achieved after 0.01 mg and after 10 mg/kg. Doses of corticosterone of 0.005 mg/kg and in a range of 0.05-0.30 mg/kg were ineffective. Corticosterone in a dose of 0.01 mg/kg (s.c.) had suppressant effects on the adrenalectomy-induced increase in the sensitivity to antinociception induced by morphine when given prior to morphine (60, 30, and 5 min) as well as after the injection of morphine (before the 1st and the 2nd testing on the hot-plate, 15 and 5 min, resp.). Intracerebroventricularly (i.c.v.) injected morphine and .beta.-endorphin also displayed the hypersensitivity to the analgesic effect in adrenalectomized rats which in both cases was suppressed by 0.01 **mg**/kg of **corticosterone** given s.c. 5 min prior to administration of the **opiate**. Aldosterone (0.3 mg/kg, s.c.) did not affect the adrenalectomy-induced morphine analgesia, but antagonized the effect obsd. with the small dose of corticosterone. The glucocorticoid antagonist RU 38486 injected i.c.v. to sham-adrenalectomized rats potentiated the antinociception induced by morphine.

The findings implicate 2 types of corticosteroid receptors in the biphasic modulation of the antinociceptive effect of opiates.

AB Adrenalectomy sensitized rats to the analgesic effect of morphine and .beta.-endorphin. Replacement therapy (chronic and acute) with corticosterone, dexamethasone, or RU 28362 (glucocorticoid receptor agonist) effectively reversed the increase in the sensitivity to the analgesic effect of peripherally injected morphine (5 mg/kg i.p.) induced by adrenalectomy to the level of sham-operated animals. Glucocorticosteroids administered to nonadrenalectomized rats did not change the sensitivity to morphine. Corticosterone had a biphasic, dose-dependent effect; the most significant attenuation of the hypersensitivity to morphine-induced antinociception in adrenalectomized rats was achieved after 0.01 mg and after 10 mg/kg. Doses of corticosterone of 0.005 mg/kg and in a range of 0.05-0.30 mg/kg were ineffective. Corticosterone in a dose of 0.01 mg/kg (s.c.) had suppressant effects on the adrenalectomy-induced increase in the sensitivity to antinociception induced by morphine when given prior to morphine (60, 30, and 5 min) as well as after the injection of morphine (before the 1st and the 2nd testing on the hot-plate, 15 and 5 min,